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10/566,821	03/16/2006	Jochen Kumlehn	13173-00023-US	7466
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CONNOLLY BOVE LODGE & HUTZ, LLP			EXAMINER	
P O BOX 2207			ZHENG, LI	
WILMINGTON, DE 19899				
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Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Office Action Summary	Application No. 10/566,821	Applicant(s) KUMLEHN, JOCHEN	
	Examiner Li Zheng	Art Unit 1638	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

- 1) ☒ Responsive to communication(s) filed on 05 July 2007.
- 2a) ☐ This action is **FINAL**. 2b) ☒ This action is non-final.
- 3) ☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

- 4) ☒ Claim(s) 1-12 is/are pending in the application.
- 4a) Of the above claim(s) 9-10 is/are withdrawn from consideration.
- 5) ☐ Claim(s) _____ is/are allowed.
- 6) ☒ Claim(s) 1-8, 11 and 12 is/are rejected.
- 7) ☐ Claim(s) _____ is/are objected to.
- 8) ☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

- 9) ☒ The specification is objected to by the Examiner.
- 10) ☒ The drawing(s) filed on 31 January 2006 is/are: a) ☒ accepted or b) ☐ objected to by the Examiner.
Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).
Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).
- 11) ☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

- 12) ☒ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).
- a) ☐ All b) ☐ Some * c) ☒ None of:
1. ☐ Certified copies of the priority documents have been received.
 2. ☐ Certified copies of the priority documents have been received in Application No. _____.
 3. ☒ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).
- * See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

- | | |
|---|---|
| 1) <input checked="" type="checkbox"/> Notice of References Cited (PTO-892) | 4) <input type="checkbox"/> Interview Summary (PTO-413)
Paper No(s)/Mail Date. _____ |
| 2) <input type="checkbox"/> Notice of Draftsperson's Patent Drawing Review (PTO-948) | 5) <input type="checkbox"/> Notice of Informal Patent Application |
| 3) <input checked="" type="checkbox"/> Information Disclosure Statement(s) (PTO/SB/08)
Paper No(s)/Mail Date <u>3/16/2006; 1/31/2006</u> | 6) <input type="checkbox"/> Other: _____ |

DETAILED ACTION

1. Claims 1-12 are pending.

Election/Restrictions

2. Applicant's election with traverse of Group I, claims 1-4, 7-8 and 11-12, in the reply filed on 7/5/2007 is acknowledged. Applicants traverse all of the restriction requirements.

Applicants contend that the reference that the Office presented does not disclose the method of the invention as claimed. Applicants particularly contend that the reference does not teach isolation of zygote that becomes substantially free from its naturally surrounding tissue (response, paragraph bridging pages 5-6).

The office contends that the isolated zygote of the reference is considered substantially free of its naturally surrounding tissue, given the undefined term "substantially". However, the restriction requirement between Group I and Group II-III are withdrawn due to claim amendment.

Applicants are advised that since the restrictions between Groups I-III are withdrawn, if any claim(s) that include(s) the limitation of the examined claims is/are presented in a continuation or divisional application, the claim of the application may be subject to a provisional statutory and/or nonstatutory double patenting rejection over the

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claims of the instant application. Where a restriction requirement is withdrawn, the provisions of 35 U.S.C. 121 no longer apply. MPEP804.01.

Claims 9-10 are withdrawn from consideration because they are drawn to non-elected subject matter.

Claims 1-8 and 11-12 are examined on the merits.

The requirement is deemed proper and is therefore made FINAL.

Specification

3. The use of the trademarks, for example, "Timentin™", "Glyphosate®", "Bioloophos®", "Dalapon®", "Bromoxynil®", and "Gelritel®", have been noted in this application (page 34, Table 1; page 28; and page 22). They should be capitalized wherever they appear and be accompanied by the generic terminology.

Although the use of trademarks is permissible in patent applications, the proprietary nature of the marks should be respected and every effort made to prevent their use in any manner which might adversely affect their validity as trademarks.

4. The specification is objected to because the blank space between pages 23-24 needs to be removed.

Claim Rejections - 35 USC § 112

The following is a quotation of the second paragraph of 35 U.S.C. 112:

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The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

5. Claim 1-8 and 11-12 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

In claim 1, the recitation, "substantially", renders the claim indefinite. The recitation is a relative term with no definite meaning. It is unclear what kind of isolated zygote is considered substantially free from surrounding tissues and how much attached surrounding tissue is allowed. The meets and bounds are not clear.

Scope of Enablement

The following is a quotation of the first paragraph of 35 U.S.C. 112:

The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

6. Claims 1-8 and 11-12 are rejected under 35 U.S.C. 112, first paragraph, because the specification, while being enabling for Agrobacterium-mediated transformation of wheat using isolated zygotes free from its naturally surrounding tissue and a feeder system comprising a culture of isolated immature pollen or pistil, does not reasonably provide enablement for using the claimed method to transform any Gramineae plant. The specification does not enable any person skilled in the art to which it pertains, or

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with which it is most nearly connected, to practice the invention commensurate in scope with these claims.

The claimed invention is not supported by an enabling disclosure taking into account the *Wands* factors. *In re Wands*, 858/F.2d 731, 8 USPQ2d 1400 (Fed. Cir. 1988). *In re Wands* lists a number of factors for determining whether or not undue experimentation would be required by one skilled in the art to make and/or use the invention. These factors are: the quantity of experimentation necessary, the amount of direction or guidance presented, the presence or absence of working examples of the invention, the nature of the invention, the state of the prior art, the relative skill of those in the art, the predictability or unpredictability of the art, and the breadth of the claim.

The claims are drawn to a method for transforming a Gramineae plant using Agrobacterium-mediated transformation and isolated zygotes substantially free from its naturally surrounding tissue.

The Office interprets that the claimed genus encompasses any Gramineae plant.

The specification teaches a method to isolate wheat zygotes and Barley immature pollen culture (page 31-page 32, line 35). The specification also teaches co-culture of isolated wheat zygotes with Agrobacterium and early embryonic development (page 33, lines 1-36). The specification further teaches regeneration and analysis of transgenic plants from isolated wheat zygotes co-cultivated with Agrobacteria (page 33, lines 39-44).

However, as taught by the specification the method is applicable to wheat because the wheat embryo sac is not as tightly embedded in nucellus tissue as the

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maize embryo sac. Therefore the isolation method taught in the specification is unlikely working for maize (specification, page 31, lines 43-46).

Further, plant transformation procedures employing plant tissue culture protocols are unpredictable. "Plant transformation is an art because of the unique culture conditions required for each crop species. To accommodate a genotype or species that has not been manipulated in culture previously, one must either adapt an established protocol or create a new one" (Hansen et. al., 1999, Trends in plant Science, vol 4, pages 226-231, see page 230). Therefore it is unpredictable that transformation protocols and methods that work for exemplified wheat would function as desired for any plant in the Gramineae family.

Further still, the specification does not provide guidance on plant regeneration from isolated zygotes for plants other than wheat. Tisserat (1985, in Plant Cell Culture, ed R.A. Dixon, IRL Press, Oxford, pages 79-90) teaches that the regeneration of plants from explants is unpredictable, and explant selection is critical for successful plant regeneration (page 80, Table 1, page 82, and Table 4, pages 85-90).

Without further guidance, undue experimentation would be required for a person skilled in the art to develop unexemplified techniques to isolate zygotes free from surrounding tissues from any Gramineae plant including maize of which embryo sac is tightly embedded in nucellus tissue, to regenerate the transformed zygotes with unexemplified feeder system, and to test the fertility of the transformed plant. See *Genentech Inc. v. Novo Nordisk, A/S* (CA FC) 42 USPQ2d 1001 (Fed. Cir. 1997),

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which teaches that "the specification, not the knowledge of one skilled in the art" must supply the enabling aspects of the invention.

Therefore, given the claim breadth, lack of further guidance and additional working example, unpredictability of the art, undue experimentation would be required for a person skilled in the art to practice the invention in full scope.

Claim Rejections - 35 USC § 103

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

(a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negated by the manner in which the invention was made.

7. Claims 1-6 and 11-12 are rejected under 35 U.S.C. 103(a) as being unpatentable over Chen et al. (1997, WO 97/48814) in view of Kumlehn et al. (1997, The Plant Journal 12:1473-1479).

The claims are drawn to a method for producing a transgenic Gramineae plant comprising the steps of: (a) isolating a zygote from a Gramineae plant to be transformed in a way that said isolated zygote becomes substantially free from its naturally surrounding tissue; (b) introducing a DNA composition comprising a genetic component into the genome of said Gramineae plant, wherein said introduction is mediated by Agrobacterium transformation into said isolated zygote; (c) regenerating Gramineae plants from said zygotes which have received said genetic component; and (d)

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identifying a fertile, transgenic Gramineae plant whose genome has been altered through the stable introduction of said genetic component; or wherein the Gramineae plant is regenerated from said isolated zygote by a method comprising co-cultivating said isolated zygote and/or a zygotic embryo derived therefrom with a feeder system; or wherein the feeder system comprises at least one of a culture of androgenetically developing barley pollen and a culture of wheat or barley pistils; or wherein said method does not comprise a step which leads to dedifferentiation of the zygote or a zygote-derived embryo; wherein said genetic component comprises an expression cassette comprising a nucleic acid sequence operably linked to a promoter active in said Gramineae plant, wherein expression of said nucleic acid sequence; or wherein the pH of the medium used during co-cultivation of the isolated zygote with *Agrobacterium* is kept in a range from about 5.8 to about 6.0.

Chen et al. teach a method for producing fertile transgenic wheat plant comprising: a) isolate wheat zygotic embryo; b) transforming said embryo with *Agrobacterium* comprising a DNA composition containing gene of interest; c) identifying or selecting a transformed cell line; and d) regenerating a fertile transgenic wheat plant therefrom, wherein said DNA is transmitted through a complete sexual cycle of said transgenic plant to its progeny, wherein said progeny comprise a selectable marker (claims 14). Chen et al. also teach the binary vector containing *nptII* gene under the control of a functional promoter (Figure 9).

Chen et al. do not teach a transformation method using isolated zygotes; or wherein the Gramineae plant is regenerated from said isolated zygote by a method

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comprising co-cultivating said isolated zygote and/or a zygotic embryo derived therefrom with a feeder system; or wherein the feeder system comprises at least one of a culture of androgenetically developing barley pollen and a culture of wheat or barley pistils; or wherein co-cultivation of the zygotes and the feeder system are employed already during Agrobacterium co-cultivation in a way that the co-cultivation culture of the zygotes and Agrobacterium is physically separated from the feeder system to prevent contact of the Agrobacteria with the feeder system but to allow exchange of growth factors, proteins, media components, and other low molecular weight compounds; or wherein said method does not comprise a step which leads to dedifferentiation of the zygote or a zygote-derived embryo; wherein said genetic component comprises an expression cassette comprising a nucleic acid sequence operably linked to a promoter active in said Gramineae plant, wherein expression of said nucleic acid sequence ; or wherein the pH of the medium used during co-cultivation of the isolated zygote with Agrobacterium is kept in a range from about 5.8 to about 6.0.

Kumlehn et al. teach a method of isolation wheat zygotes and regeneration of a fertile wheat plant from isolated zygotes (abstract). Kumlehn et al. further teach the direct embryogenesis and plant regeneration are performed by implantation of individual wheat zygotes into cultured ovules of wheat or barley (abstract; also page 1475, Figure 1). Kumlehn et al. further teach that this novel approach constitutes an alternative plant regeneration system for isolated zygotes and a valuable tool for further research and that isolated wheat zygotes are suitable targets for genetic transformation (page 1477, 3rd paragraph of the right column). Kumlehn et al. also teach that it is known in the art

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that embryogenesis can be induced by co-cultivation of isolated zygotes with microspore-derived embryogenic structures of barley (page 1473, 1st paragraph of left column).

Given the recognition of those of ordinary skill in the art of the value of the wheat transformation method of Chen et al., it would have been obvious for a person with ordinary skill in the art to modify the Agrobacterium mediated transformation method of Chan et al. by using isolated zygotes of Kumlehn et al. and further using the regeneration method of Kumlehn et al. to regenerate fertile wheat transgenic plant. One would be motivated to do so given the teaching of Kumlehn et al. that isolated wheat zygotes are suitable targets for genetic transformation and obtaining alternative transformation method for commercially important crops such as wheat is highly desirable.

Although the combined teaching does not teach the feeder comprising comprises at least one of a culture of androgenetically developing barley pollen and a culture of wheat or barley pistils, the cultured ovules of wheat or barley of Kumlehn et al. are from a culture of wheat or barley pistils.

Although the combined teaching does not teach the pH of the medium used during co-cultivation of the isolated zygote with Agrobacterium is kept in a range from about 5.8 to about 6.0, it is empirically determined and is an optimization of process parameters.

Thus the claimed invention would have been *prima facie* obvious as a whole to one of ordinary skill in the art at the time it was made, especially in the absence of evidence to the contrary.

8. Claims 1-8 and 11-12 are rejected under 35 U.S.C. 103(a) as being unpatentable over Chen et al. (1997, WO 97/48814) in view of Kumlehn et al. (1997, The Plant Journal 12:1473-1479) as for claims 1-5, 11-12, further in view of Holm et al. (1994, The Plant Cell 8:531-543).

Claims 1-6 and 11-12 are discussed as above.

Claims 7-8 recite further limitations of that co-cultivation of the zygotes and the feeder system are employed already during Agrobacterium co-cultivation in a way that the co-cultivation culture of the zygotes and Agrobacterium is physically separated from the feeder system to prevent contact of the Agrobacteria with the feeder system but to allow exchange of growth factors, proteins, media components, and other low molecular weight compounds.

The teachings of Chen et al. and Kumlehn et al. are discussed above.

Chen et al. and Kumlehn et al. do not teach co-cultivation of the zygotes and the feeder system are employed already during Agrobacterium co-cultivation in a way that the co-cultivation culture of the zygotes and Agrobacterium is physically separated from the feeder system to prevent contact of the Agrobacteria with the feeder system but to allow exchange of growth factors, proteins, media components, and other low molecular weight compounds.

Holm et al. teach several methods for co-cultivation wherein zygotes is physically separated from the microspore culture (feeder system) by using a Transwell insert, which prevents contact of the zygotes with the feeder system but to allow exchange of nutrients and other compounds (page 534, 3rd paragraph of right column).

Given the recognition of those of ordinary skill in the art of the value of above mentioned modified wheat transformation method of Chen et al. and Kumlehn et al. it would have been obvious for a person with ordinary skill in the art to further adopt the cocultivation method as taught by Holm et al. by immerse the Transwell insert containing zygotes and Agrobacterium into liquid wheat or barley pistil culture. One skilled in the art would have obviously made such modification because this is merely a design choice with reasonable expectation of success.

Although the combined teaching does not teach the pH of the medium used during co-cultivation of the isolated zygote with Agrobacterium is kept in a range from about 5.8 to about 6.0, it is empirically determined and is an optimization of process parameters.

Thus the claimed invention would have been *prima facie* obvious as a whole to one of ordinary skill in the art at the time it was made, especially in the absence of evidence to the contrary.

Conclusion

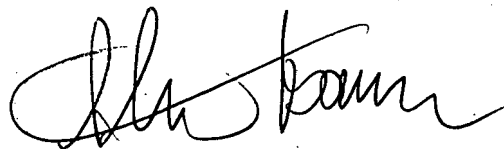
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No claim is allowed.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Li Zheng whose telephone number is 571-272-8031. The examiner can normally be reached on Monday through Friday 9:00 AM - 5:30 PM EST.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Anne Marie Grunberg can be reached on 571-272-0975. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see <http://pair-direct.uspto.gov>. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).

A handwritten signature in black ink, appearing to read 'Stuart F. Baum', is written over a horizontal line.

STUART F BAUM, PH.D.
PRIMARY EXAMINER

